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TO: Ralph J Gitomer Location: rem-3D65/3C18 Art Unit: 1655 Wednesday, October 26, 2005 Case Serial Number: 10/606038	From: Alex Waclawiw Location: Biotech-Chem Library Rem 1A71 Phone: 272-2534 Alexandra.waclawiw@uspto.gov

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FILE 'WPIDS' ENTERED AT 14:03:25 ON 26 OCT 2005

L2 76 S LING K?/AU
L3 1 S DOUGHMAN R?/AU
L4 1540 S ANDERSON R?/AU
L5 1615 S L2-4
L6 2 S PIPKI OR PIPK
L7 1 S L6 (4A) 661
L8 1 S PHOSPHATIDYLINOSITOL PHOSPHATE KINASE
L9 2 S L6-8
L10 1 S L5 AND L9
L11 3 S L5 AND PHOSPHATIDYL?
L12 3 S L10 OR L11
L13 4 S L9 OR L10 OR L11

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=> fil wpids
FILE 'WPIDS' ENTERED AT 14:06:42 ON 26 OCT 2005
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FILE LAST UPDATED:          24 OCT 2005      <20051024/UP>
MOST RECENT DERWENT UPDATE:     200568        <200568/DW>
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    FOR DETAILS. <<<

=> d que l13
L2            76 SEA FILE=WPIDS ABB=ON  PLU=ON  LING K?/AU
L3             1 SEA FILE=WPIDS ABB=ON  PLU=ON  DOUGHMAN R?/AU
L4          1540 SEA FILE=WPIDS ABB=ON  PLU=ON  ANDERSON R?/AU
L5          1615 SEA FILE=WPIDS ABB=ON  PLU=ON  (L2 OR L3 OR L4)
L6             2 SEA FILE=WPIDS ABB=ON  PLU=ON  PIPKI OR PIPK
L7             1 SEA FILE=WPIDS ABB=ON  PLU=ON  L6 (4A) 661
L8             1 SEA FILE=WPIDS ABB=ON  PLU=ON  PHOSPHATIDYLINOSITOL PHOSPHATE
                 KINASE
L9             2 SEA FILE=WPIDS ABB=ON  PLU=ON  (L6 OR L7 OR L8)
L10            1 SEA FILE=WPIDS ABB=ON  PLU=ON  L5 AND L9
L11            3 SEA FILE=WPIDS ABB=ON  PLU=ON  L5 AND PHOSPHATIDYL?
L13            4 SEA FILE=WPIDS ABB=ON  PLU=ON  L9 OR L10 OR L11

=> d .wp 1-4

L13  ANSWER 1 OF 4  WPIDS  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2005-079421 [09]   WPIDS
DNN  N2005-069799       DNC C2005-027690
TI   Identification of an agent for modulating the activity of
     phosphatidylinositol phosphate kinase isoform
     gamma 661, comprises contacting isoform gamma 661 with a test agent and
     detecting activity of the isoform.
DC   B04 D16 S03
IN   ANDERSON, R A; DOUGHMAN, R L; LING, K
PA   (ANDE-I) ANDERSON R A; (DOUG-I) DOUGHMAN R L; (LING-I) LING K
CYC  1
PI   US 2004265295   A1 20041230 (200509)*      47
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ADT US 2004265295 A1 US 2003-606038 20030625
PRAI US 2003-606038 20030625
AB US2004265295 A UPAB: 20050207
NOVELTY - Identification of an agent (I) that modulates the activity of **phosphatidylinositol phosphate kinase** isoform gamma **661** (**PIPKI** gamma **661**) (II), comprises contacting (II) with a test agent in the presence of a protein, and detecting the activity of (II) (where change in the activity of (II) compared to a control is indicative of the agent that modulates the activity of (II)).

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for identification of an agent that modulates cell focal adhesion assembly comprises contacting a cell which lacks active (II) or which over expresses (II) with a test agent and measuring the adherence of the cell to a surface (where a difference in the presence of the test agent compared to the absence of the test agent is indicative of the agent modulating cell focal adhesion assembly).

ACTIVITY - Cytostatic; Vulnerary; Analgesic; Immunomodulatory. Tests details are described but no results given.

MECHANISM OF ACTION - **Phosphatidylinositol phosphate kinase** isoform gamma **661** (**PIPKI** gamma **661**) modulator.

USE - (I) Is useful to treat or prevent cell migration mediated conditions or diseases (claimed). (I) Is also useful to treat conditions or diseases involving cancer invasiveness, cancer metastasis, wound healing, immune responses or neuronal development.

Dwg.0/3
TECH UPTX: 20050207
TECHNOLOGY FOCUS - PHARMACEUTICALS - Preferred Method: The proteins are Src or FAK and (I) modulates their activity.

L13 ANSWER 2 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2004-011486 [01] WPIDS
CR 2003-221525 [21]
DNN N2004-008482 DNC C2004-003194
TI Apparatus for detecting plaque in a blood vessel using selectively targeted fluorescent or radiolabeled compositions, useful for treating active atheromatous or vulnerable plaques, particularly in atherosclerotic heart disease.
DC A96 B04 D16 K08 P31 S03 S05
IN **ANDERSON, R**; DAGHIGHIAN, F; ELMALEH, D R; FISCHMAN, A; HAMBLIN, M R; HASAN, T; MULLER, J; TAWAKOL, A
PA (GEHO) GEN HOSPITAL CORP
CYC 102
PI WO 2003077723 A2 20030925 (200401)* EN 139
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
AU 2002360488 A1 20030929 (200432)
EP 1575414 A2 20050921 (200562) EN
R: AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LU MC NL PT SE SI SK TR
ADT WO 2003077723 A2 WO 2002-US38852 20021203; AU 2002360488 A1 AU 2002-360488 20021203; EP 1575414 A2 EP 2002-795747 20021203, WO 2002-US38852 20021203
FDT AU 2002360488 A1 Based on WO 2003077723; EP 1575414 A2 Based on WO

2003077723
PRAI US 2002-216026 20020809; US 2002-365673P 20020315;
US 2002-163744 20020604; US 2002-215600 20020809;
US 2002-215958 20020809
AB WO2003077723 A UPAB: 20050928
NOVELTY - An apparatus for detecting plaque in a blood vessel, is new.

DETAILED DESCRIPTION - An apparatus for detecting plaque in a blood vessel comprises a light emitter operable to emit light having a first predetermined wavelength, and a light detector operable to detect light having a second predetermined wavelength, where a predetermined amount of at least one fluorescent composition is administered to the blood vessel, and light having the first predetermined wavelength causes the fluorescent composition to localize to a plaque that emits light having the second predetermined wavelength.

INDEPENDENT CLAIMS are also included for the following:

(1) an apparatus for detecting and treating plaque in a blood vessel, comprising a probe operable to be inserted in the blood vessel, the probe including a detector operable to detect heat from the plaque, and a light emitter operable to emit light having a predetermined wavelength, where light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species, stabilizing the target plaque;

(2) a method of detecting an active atheromatous or vulnerable plaque in a subject, comprising administering a beta-emitting composition, localizing the composition to the active atheromatous or vulnerable plaque, detecting a signal from the beta-emitting composition, and identifying the active atheromatous or vulnerable plaque and/or administering a suitable treatment; and

(3) a method of detecting and treating an active atheromatous or vulnerable plaque in a subject, comprising administering a beta-emitting composition, localizing the composition to the active atheromatous or vulnerable plaque, detecting a signal from the beta-emitting composition, and identifying the active atheromatous or vulnerable plaque and administering a suitable treatment to it.

ACTIVITY - Antiarteriosclerotic. An intravascular fluorescence catheter that efficiently localized a fluorescence signal from a vulnerable plaque in the rabbit coronary through blood was developed. A therapeutic intravascular light delivery system was developed that illuminated plaques through flowing blood with the appropriate wavelength, fluence and fluence rate of light, achieving the desired therapeutic effect. PDT in rabbit aorta was demonstrated to be possible in vivo in living rabbits through blood flowing without undue harm to the rabbits and with no short-term toxicity.

MECHANISM OF ACTION - None given.

USE - The methods and compositions of the present invention are useful for diagnosing and/or treating an active atheromatous or vulnerable plaque, particularly in atherosclerotic heart disease.

DESCRIPTION OF DRAWING(S) - The drawing shows a detection/treatment system for detecting and/or targeting and/or treating vulnerable plaque.

Detection and Treatment System 100
Control Unit 105
Detection and Treatment Unit 110
Light Source/Laser 113
Detection/Treatment Device 115
Blood Vessel 120
Computing Device 125
Dwg.1/23
TECH UPTX: 20040102
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Apparatus: The light emitter

and the light detector are included in a probe that is operable to be inserted into the blood vessel. The apparatus further comprises a therapeutic light emitter operable to emit light having a third predetermined wavelength, where a therapeutically effective amount of at least one photosensitizer composition is administered to the blood vessel, the photosensitizer composition localizes to target plaque, and light having the third predetermined wavelength causes the photosensitizer composition to produce a phototoxic species, which stabilizes the target plaque. The apparatus also has a therapeutic light emitter operable to emit light having the third predetermined wavelength at a predetermined power level, where light having the third predetermined wavelength at the predetermined power level causes the photosensitizer composition to produce the phototoxic species in an amount that does not induce necrosis of the cells comprising the target plaque. The third predetermined wavelength is 405 nm. The first predetermined wavelength is 337 nm, and the second predetermined wavelength is between 666-668 nm. The apparatus further comprises an inflatable vessel coupled to the light detector, whereby the light detector is moved towards a wall of the blood vessel by inflating the inflatable vessel, where the inflatable vessel contains saline, and also comprising an external unit, where the inflatable vessel and the light detector are retractable into and extendible out from the external unit. The apparatus also comprises the external unit comprising an elastic structure coupled to the light detector, the elastic structure and the light detector being retractable into and extendible out from the external unit, whereby the elastic structure moves the light detector towards a wall of the blood vessel when extended out from the external unit. The apparatus also has a detector operable to detect heat or to detect a signal that includes a radioactive signal emitted from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, where the radioactive signal includes gamma or beta rays. The detector includes a first predetermined sensitivity to beta rays and a second predetermined sensitivity to gamma rays, where the first predetermined sensitivity is equal to 100 times the second predetermined sensitivity. The signal includes an infrared signal. The detector also includes an image producing camera detector. The apparatus alternatively comprises means for emitting light having a first predetermined wavelength, and means for detecting light having a second predetermined wavelength, where a predetermined amount of at least one fluorescent composition is administered to the blood vessel, the fluorescent composition localizes to the plaque, and light having the first predetermined wavelength causes the fluorescent composition localized to the plaque to emit light having the second predetermined wavelength. The plaque or target plaque in any of the apparatus cited above includes active atheromatous or vulnerable plaque. The apparatus for detecting and treating plaque in a blood vessel also comprises a probe operable to be inserted in the blood vessel, the probe including a detector operable to detect gamma rays from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, and a light emitter operable to emit light having a predetermined wavelength, whereby light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species, stabilizing the target plaque. The detector includes a first predetermined sensitivity to beta rays and a second predetermined sensitivity to gamma rays. The first predetermined sensitivity is equal to 100 times the second predetermined sensitivity. The apparatus also comprises means for detecting heat from the plaque, and means for emitting light having a predetermined wavelength, where light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species,

stabilizing the target plaque, and alternatively means for detecting gamma rays from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, and means for emitting light having a predetermined wavelength, whereby light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species, stabilizing the target plaque. The apparatus further comprises a detector operable to detect beta rays from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, and a light emitter operable to emit light having a predetermined wavelength, whereby light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species, stabilizing the target plaque, and also comprising means for detecting beta rays from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, and means for emitting light having a predetermined wavelength, whereby light having the predetermined wavelength causes a photosensitizer composition administered and localized to target plaque to produce a phototoxic species, stabilizing the target plaque. The apparatus also has probe operable to be inserted in the blood vessel, the probe including a detector operable to detect beta rays from a composition comprising a radiolabeled molecular carrier administered and localized to the plaque, and a delivery unit operable to deliver a therapeutic compound to the plaque, the therapeutic compound stabilizing target plaque. The delivery unit includes a stent, and/or an inflatable vessel, and is moved towards a wall of the blood vessel by inflating the inflatable vessel that contains a transparent, non-toxic fluid. The apparatus further comprises an external unit, where the stent is retractable into and extendible out from the external unit, and where the external unit contains the therapeutic compound, and where the therapeutic compound is applied onto the stent each time the stent is retracted into the external unit. The detector is operable to detect gamma rays, and includes a first predetermined sensitivity to beta rays and a second predetermined sensitivity to gamma rays. The first predetermined sensitivity is equal to 100 times the second predetermined sensitivity. Preferred Method: The active atheromatous plaque detected comprises a plaque accumulating aggregated platelets and monocytes, such that greater than 50% stenosis is achieved, and where the thin fibrous cap is greater than 200 microns thick. The active atheromatous plaque comprises lipids and inflammatory ceils selected from smooth muscle ceils, leukocytes, lymphocytes, monocytes, macrophages, foam cells, mast cells, endothelial cells, platelets, erythrocytes and polymorphonuclear cells. The lymphocytes comprise B-lymphocytes and T-lymphocytes. The polymorphonuclear cells comprise granulocytes and neutrophils. The inflammatory cells comprise macrophages and/or monocytes. The beta-emitting composition comprises a beta-emitting agent selected from 18F-Fluorodeoxyglucose, I131, Re186 and Re188 coupled to a molecular carrier that targets inflammatory components selected from inflammatory cells, lipids, procoagulants and agents that promote inhibition of extracellular matrix production or degradation of extracellular matrix. The molecular carrier is selected from the group consisting of serum proteins, receptor ligands, microspheres, liposomes, antibodies, growth factors, peptides, hormones and lipoproteins, and binds to a scavenger receptor. The molecular carrier is also selected from maleylated albumin, daunorubicin, doxorubicin, oxidized low density lipoprotein, acetylated low density lipoprotein, oxidized high density lipoprotein, malondialdehyde treated proteins, formaldehyde treated albumin, glycated albumin, polyinosinic acid, glycated lipoproteins, dextran sulfate, anionic phospholipids, fucoidin, carrageenan, polyvinyl sulfate and monoclonal antibodies that recognize CD11b, CD11c, CD13, CD14, CD16a, CD32

or CD68. The anionic phospholipid is **phosphatidyl** serine. The molecular carrier targets the beta-emitting composition to a T lymphocyte, where the molecular carrier is selected from monoclonal antibodies that recognize CD1, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD25, CD28, CD44 and CD71 and transferrin. The molecular carrier also targets the beta-emitting composition to lipids of the active atheromatous plaque, and comprises hydrophobic vehicles selected from liposomes, cremaphor EL, PEG/solvent mixtures, iodized castor oil, nanoparticles and micellar preparations. The liposomes contain cholesterol or cardiolipin. The molecular carrier also targets the beta-emitting composition to macrophages, or to a macrophage biomolecule selected from tenascin C, tissue factor, tissue inhibitor of MMP 1, tissue inhibitor of MMP 2, oxidized LDL receptor, heme oxygenase-1, human cartilage gp-39, IL-6, IL-6 receptor, IL-10, IL-10 receptor, lectin-like oxidized LDL-receptor, monocyte inflammatory protein-1, monocyte inflammatory protein-1 receptor and macrophage chemoattractant protein- 1 receptor. The molecular carrier also targets the beta-emitting composition to a T cell biomolecule selected from IL-10, IL-10 receptor, monocyte inflammatory protein-I, monocyte inflammatory protein-1 receptor and transferrin. The molecular carrier also targets the beta-emitting composition to foam cells, or to a protease that degrades extracellular matrix, where the protease is a metalloproteinase. The molecular carrier is a monoclonal antibody that binds to an epitope on a protease. The vulnerable plaque comprises inflammatory components, a large lipid pool, and a thin fibrous cap that is less than 150 or 100 microns thick. The inflammatory components are inflammatory cells, lipids, procoagulants and agents that promote inhibition of extracellular matrix production or degradation of extracellular matrix. The inflammatory cells are smooth muscle cells, leukocytes, lymphocytes, monocytes, macrophages, foam ceils, mast cells, endothelial ceils, platelets, erythrocytes or polymorphonuclear cells. The lymphocytes comprise B-lymphocytes and T-lymphocytes. The polymorphonuclear cells comprise granulocytes and neutrophils. The lipid content is greater than 10% or 25%. Detecting and treating an active atheromatous or vulnerable plaque further comprises administering a detectable amount of at least one beta-emitting composition, where the beta-emitting composition is localized to an active atheromatous or vulnerable plaque, administering at least one photosensitizer composition, where the photosensitizer composition is localized to the plaque, detecting a signal from the beta-emitting composition, identifying the plaque, light activating the photosensitizer composition at the site of the plaque to produce a phototoxic species, and stabilizing the active atheromatous or vulnerable plaque against rupture. The photosensitizer is chlorine6. The light is administered in a 20-500, 50-300 or 100-200 J/cm dose. The method also comprises administering a beta-emitting composition comprising a beta-emitting agent coupled to a molecular carrier, where the beta-emitting composition is localized to an active atheromatous or vulnerable plaque, administering a photosensitizer composition comprising a photosensitizer coupled to a molecular carrier, where the photosensitizer composition is localized to the active atheromatous or vulnerable plaque, detecting a signal from the beta-emitting composition, identifying the active atheromatous or vulnerable plaque, light activating the photosensitizer at the site of the active atheromatous or vulnerable plaque to produce a phototoxic species, and stabilizing the active atheromatous or vulnerable plaque against rupture. The method alternatively comprises administering a beta-emitting composition, localizing the composition to the active atheromatous or vulnerable plaque, detecting a signal from the beta-emitting composition, employing one or more additional means to identify the plaque, and identifying the active atheromatous or vulnerable plaque, or comprising administering a radiolabeled composition, localizing the composition to

the active atheromatous or vulnerable plaque, detecting a signal from the radiolabeled composition, identifying the active atheromatous or vulnerable plaque.

L13 ANSWER 3 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 2003-221525 [21] WPIDS
CR 2004-011486 [01]
DNC C2003-056296
TI Detecting vulnerable plaque in subject by administering fluorescent composition, localizing the composition to vulnerable plaque, and light activating the composition to illuminate the plaque, and identifying plaque.
DC B04 D16 P34
IN DAGHIGHIAN, F; ELMALEH, D; **ANDERSON, R**; FISCHMAN, A; HAMBLIN, M R; HASAN, T; MULLER, J; TAWAKOL, A; HASSAN, T
PA (DAGH-I) DAGHIGHIAN F; (ELMA-I) ELMALEH D; (ANDE-I) ANDERSON R; (FISC-I) FISCHMAN A; (HAMB-I) HAMBLIN M R; (HASA-I) HASAN T; (MULL-I) MULLER J; (TAWA-I) TAWAKOL A; (HASS-I) HASSAN T; (GEHO) GEN HOSPITAL CORP
CYC 101
PI WO 2003003975 A2 20030116 (200321)* EN 94
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZW
US 2003055307 A1 20030320 (200323)
US 2003082105 A1 20030501 (200331)
US 2003103995 A1 20030605 (200339)
EP 1401479 A2 20040331 (200424) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR
AU 2002327180 A1 20030121 (200452)
JP 2005502618 W 20050127 (200510) 151
ADT WO 2003003975 A2 WO 2002-US18472 20020604; US 2003055307 A1 Provisional US 2001-295627P 20010604, Provisional US 2002-365673P 20020315, CIP of US 2002-163744 20020604, US 2002-215600 20020809, Div ex US 2002-215958 20020809; US 2003082105 A1 Provisional US 2001-295627P 20010604, Provisional US 2002-365673P 20020315, CIP of US 2002-163744 20020604, US 2002-215958 20020809; US 2003103995 A1 Provisional US 2001-295627P 20010604, Provisional US 2002-365673P 20020315, US 2002-163744 20020604; EP 1401479 A2 EP 2002-763205 20020604, WO 2002-US18472 20020604; AU 2002327180 A1 AU 2002-327180 20020604; JP 2005502618 W WO 2002-US18472 20020604, JP 2003-509989 20020604
FDT EP 1401479 A2 Based on WO 2003003975; AU 2002327180 A1 Based on WO 2003003975; JP 2005502618 W Based on WO 2003003975
PRAI US 2002-365673P 20020315; US 2001-295627P 20010604; US 2002-163744 20020604; US 2002-215600 20020809; US 2002-215958 20020809
AB WO2003003975 A UPAB: 20050211
NOVELTY - Detecting (M1) a vulnerable plaque (I) in a subject involves administering a fluorescent composition, localizing the composition to (I), and light activating the composition to illuminate (I), and identifying (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) stabilizing (M2) (I) involves administering at least one photosensitizer composition, which is localized to (I), light activating the photosensitizer composition to produce a phototoxic species and

stabilizing (I) against rupture;

(2) detecting and treating (M3) (I) in a subject involves administering a detectable amount of fluorescent composition which is localized to (I), and administering at least one photosensitizer composition which is localized to (I), and light activating (I) to produce a fluorescent species, and identifying (I), and light activating the photosensitizer composition at the site of (I) to produce a phototoxic species, and stabilizing (I) against rupture;

(3) detecting and treating (M4) (I) in a subject involves administering a composition comprising a radiolabeled macromolecular carrier, and localizing the composition to (I) and measuring radioactive signal, administering at least one photosensitizer composition which is localized to (I), and light activating the photosensitizer composition at the site of (I) to produce a phototoxic species, and stabilizing (I) against rupture;

(4) apparatus (II) for detecting (I) in a blood vessel, comprises a light emitter (113) operable to emit light having a first predetermined wavelength, and a light detector (115) operable to detect light having a second predetermined wavelength, whereby a predetermined amount of at least one fluorescent composition is administered to the blood vessel, the fluorescence composition localizes to (I), and light having the first predetermined wavelength causes the fluorescent composition localized to (I) to emit light having the second predetermined wavelength; and

(5) apparatus (III) for detecting and treating (I) in a blood vessel, comprises a detector operable to detect to emission from (I), and a light emitter operable to emit light having a predetermined wavelength, whereby light having the predetermined wavelength causes a photosensitizer composition administered and localized to (I) to produce a phototoxic species, thus stabilizing (I).

ACTIVITY - Apoptotic; Antiinflammatory; Antiatherosclerotic. No biological data given.

MECHANISM OF ACTION - Photodynamic therapy.

USE - (M1) is useful for detecting vulnerable plaque in a subject. (M2) is useful for stabilizing (I) in a subject, where (I) comprises inflammatory components, a large liquid pool and a thin fibrous cap which is less than 150 microns, preferably 100 microns thick. The inflammatory components are chosen from inflammatory cells, lipids, procoagulants and agents that promote inhibition of extracellular matrix production or degradation of extracellular matrix. The inflammatory cells are chosen from smooth muscle cells, leukocytes, lymphocytes (B or T lymphocytes), monocytes, macrophages, foam cells, mast cells, endothelial cells, platelets, erythrocytes and polymorphonuclear cells (e.g. granulocytes or neutrophils). The inflammatory cells comprises greater than 10% (preferably 25%) macrophages and/or monocytes. The lipid content comprises greater than about 10% (preferably 25%). (M3) and (M4) are useful for detecting and treating a vulnerable plaque in a subject (claimed). The methods are useful for detecting and treating thin cap fibroatheroma (vulnerable plaque).

ADVANTAGE - The light activating the photosensitizer composition to produce a phototoxic species is administered in an amount sufficient to induce apoptosis and not necrosis of the cells comprising (I) (claimed). Inducing apoptosis rather than necrosis reduces or eliminates the inflammatory response following photodynamic therapy and enhances the overall therapeutic effect. (M1) advantageously differentiates stable atheromatus lesion from vulnerable plaques.

DESCRIPTION OF DRAWING(S) - The figure shows detections/treatment system for detecting and/or targeting and/or vulnerable plaque, and the configuration of the control unit.

Light emitter 113

Light detector 115
1a, 1b/15
TECH UPTX: 20030328
TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Method: In (M1), the fluorescent composition comprises a photosensitizer, fluorescent dye, or photoactive dye coupled to a macromolecular carrier. (M1) further involves light activating the photosensitizer at the site of (I) and stabilizing (I) against rupture. In (M2), the photosensitizer comprises a photosensitizer coupled to a macromolecular carrier. The macromolecular carrier targets inflammatory cells, lipids, procoagulants and agents that promote inhibition of extracellular matrix production or degradation of extracellular matrix. The macromolecular carrier is chosen from serum proteins, receptor ligands, microspheres, liposomes, antibodies, growth factors, peptides, hormones and lipoproteins. The macromolecular carrier binds to a scavenger receptor, and is selected from maleylated albumin, daunorubicin, doxorubicin, oxidized low density lipoprotein, acetylated low density lipoprotein, oxidized high density lipoprotein, malondialdehyde treated proteins, formaldehyde treated albumin, glycated albumin, polyinosinic acid, glycated lipoproteins, dextran sulfate, anionic phospholipids, fucoidin, carrageenan, polyvinyl sulfate and monoclonal antibodies that recognize CD11b, CD11c, CD13, CD14, CD16a, CD32 or CD68. The anionic phospholipid is preferably **phosphatidyl** serine. The macromolecular carrier which targets the photosensitizer composition to a T cell (preferably a T cell biomolecule selected from IL-10, IL-10 receptor, monocyte inflammatory protein-I, monocyte inflammatory protein-I receptor and transferrin), is chosen from monoclonal antibodies that recognize CD1, CD2, CD3, CD4, CD5, CD6, CD7, CD8, CD25, CD28, CD44 and CD71 and transferrin. The macromolecular carrier which targets the photosensitizer composition to the lipids comprising the lipid pool of the atheroma, comprises a hydrophobic vehicles chosen from liposomes, cremaphor EL, polyethylene-glycol (PEG)/solvent mixtures, iodized castor oil, nanoparticles and micellar preparations. Preferably, the liposome contains cholesterol or cardiolipin. The macromolecular carrier which targets the photosensitizer composition to macrophages, preferably to a macrophage biomolecule chosen from tenascin C, tissue factor, tissue inhibitor of matrix metalloproteinase (MMP) 1, tissue inhibitor of MMP2, oxidized low density lipoprotein (LDL) receptor, heme oxygenase-1, human cartilage gp-39, interleukin (IL)-6, IL-6 receptor, IL-10, IL-10 receptor, lectin-like oxidized LDL-receptor, monocyte inflammatory protein-I, monocyte inflammatory protein-I receptor and macrophage chemoattractant protein-1 receptor. The macromolecular carrier also targets the photosensitizer composition to the foam cells, or to a protease that degrades extracellular matrix, where the protease is a metalloproteinase, and the macromolecular carrier is a monoclonal antibody that binds to an epitope on a protease. The light which activates the photosensitizer to produce a phototoxic species, further produces crosslinks in the fibrous cap. Most preferably, the photosensitizer is chlorine6.
TECHNOLOGY FOCUS - INSTRUMENTATION AND TESTING - Preferred Apparatus: In (II), the light emitter and the light detector is included into a probe, and the probe is operable to be inserted in a blood vessel. The apparatus further comprises therapeutic light emitter operable to emit light having a third predetermined wavelength, where the photosensitizer composition is administered through the blood vessel, the photosensitizer composition localizes the(II) and light having the third predetermined wavelength causes the photosensitizer composition to produce phototoxic species, which stabilizes (I). The therapeutic light emitter is preferably operable to emit light having predetermined wavelength at a predetermined power level, thereby light having the third predetermined power level causes the

photosensitizer composition to produce the phototoxic species in an amount that does not induce necrosis of cells comprising (I). The first predetermined wavelength is 337 nm, second predetermined wavelength is 666-668 nm, and the third predetermined wavelength is between 405 nm. The apparatus further comprises an implantable vessel, coupled to the light detector, whereby the light detector is moved towards a wall of the blood vessel by inflating the blood vessel. Preferably, the inflatable vessel contains saline. The apparatus further comprises an external unit, whereby the inflatable vessel and the light detector are retractable into the extendible and the external unit; and an external unit, and an elastic structure coupled to the light detector, the elastic structure and light detector being retractable into and extendible out from the external unit, whereby the elastic structure moves light detector towards the wall of the blood vessel when extended out from the external unit. In (IV), the detector is operable to detect an emission which includes heat, or includes radioactive signals from a composition comprising a radiolabeled macromolecular administered and localized to (I).

L13 ANSWER 4 OF 4 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN
AN 1993-401022 [50] WPIDS
CR 2001-263299 [27]
DNN N1999-033795
TI Image pick up apparatus for electronic still camera, copier - corrects distortion of image data by executing interpolation of image data defined by control points in accordance with three control points from among four control points.
DC S06 T01 T04
IN EBIHARA, T
PA (OLYU) OLYMPUS OPTICAL CO LTD
CYC 2
PI JP 05303634 A 19931116 (199350)* 10
US 5848197 A 19981208 (199905)B 20
JP 3093869 B2 20001003 (200051) 11
ADT JP 05303634 A JP 1992-109733 19920428; US 5848197 A Cont of US 1993-53879 19930427, Cont of US 1995-397721 19950302, US 1997-779058 19970106; JP 3093869 B2 JP 1992-109733 19920428
FDT JP 3093869 B2 Previous Publ. JP 05303634
PRAI JP 1992-109733 19920428
AB US 5848197 A UPAB: 19990203 ABEQ treated as Basic
The apparatus consists of a reading unit (1) which reads a document and outputs a corresponding electric signal to an A/D converter (2). The A/D converter converts the electrical signal into digital signal and stores it in an input image memory (3). The multiple pixels in the image data of the input image memory is reduced and thus a substantially reduced image data is output by an image reduction processor (4) and an image converter (7). The reduced image data is stored in a reduced image memory (5). The reduced image data memory is read by a control point coordinate generator (6) and x and y coordinates of four control points corresponding to the distortion of the reduced image data is generated.

The reduced image data from the image converter is corrected by a distortion correcting unit by executing the interpolation of the image data of three control points defined by the control points based on the equation, PiP=S*PiPj+t***PiPk**, QiQ=S*QiQj+t*QiQk, where PiP, PiPj, **PiPk**, QiQ, QiQj, QiQk are vectors, Pi, Pj, Pk are coordinates of three control points before conversion, Qi, Qj, Qk are coordinates of three control points after conversion, S is the coefficient of the vectors PiPj and QiQj, t is the coefficient of the vectors **PiPk** and QiQk. The corrected image data from the distortion correction unit is stored in a corrected image memory (8) and is output to an image recording

unit (9).
ADVANTAGE - Performs distortion correction and obtains flat image of characters distorted by curved surface.
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